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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/080,127	05/15/1998	ALEXANDER BLINKOVSKY	5253.200-US	9075

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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1647	23

DATE MAILED: 04/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/080,127	Blinkovsky
Examiner	**Art Unit**
Sharon L. Turner, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 1-23-02

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 170-206 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 170, 174, 177, 180, 184-189, 193, 196, and 199 is/are rejected.

7) ☒ Claim(s) 171-173, 175, 176, 178, 179, 181-183, 190-192, 194, 195, 197, 198, and 200-206 is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

Response to Amendment

1. The amendment filed 1-23-02 has been entered into the record and has been fully considered. Claims 130-169 are canceled. New Claims 170-206 are pending.

Claim Objections

2. Claim 202 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 202 depends from claim 190, 189 and 170 and shares all the characteristics thereof and therefore does not further limit as the polypeptide of claim 170 already requires the peptide to possess the characteristics recited. Claims 203-205 are also objected to as they depend from objected claim 202.

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 174, 184-188, and 193 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. This is a written description rejection.

The specification describes a single polypeptide sequence consisting of SEQ ID NO:2, which is shown to have the activities as recited in claim 170 elements I-iv/claim 184 elements a)-d) . However, the claims are directed to peptides encoded by nucleic acid sequences which hybridizes with SEQ ID NO:1 or it's complementary strand, and to fragments which exhibit amino peptidase activity. In addition, in contrast to claim 170, claims 174, 184-187 and 193 lack any structural recitations in the claims (including fragments with aminopeptidase activity) and thus encompass any structure which achieves the functional characteristics. Thus, the claims encompass all structural molecules which share the delimited functional constraints. Yet, the instant disclosure of a single polypeptide, that of SEQ ID NO:2 with the instantly disclosed specific activities, does not adequately describe the claimed genus drawn to a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the

written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a (product) DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the (product) DNA itself." Id at 1170, 25 USPQ2d at 1606."

Yet, in claims 174, 184-187 and 193 there are no distinguishing structural features noted for the subgenera of functional variants or for functional fragments. The specification describes only a singular species which falls within the subgenus but fails to describe the structural features commonly possessed by it's members or an adequate number of species which distinguish the subgenus members from others, including fragments and sequences which provide for the recited activity. Thus, as in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), the naming of the type of material generally known to exist, in absence of knowledge as to what that material consists of, is not a description of that material. the artisan can not readily envision or discern those compounds which are members and thus the functional recitation alone fails to provide adequate written description to support the genus claimed. In addition, the specification fails to delineate hybridizing sequences other than that of SEQ ID NO:1 which meet the functional constraints. It is again noted that

sequences hybridizing to SEQ ID NO:1 reveal non-coding strands unrelated to the polypeptide claimed, and thus the claims lack written description of a representative number of species of the hybridizing or fragment subgenus. In claim 188, there is no description of a suitable strain other than Aspergillus oryzae or deposited strain pEJG18, E. coli NRRL B-21677.

5. Claims 174, 184-188 and 193 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the aminopeptidase of residues 16-496 of SEQ ID NO:2, does not reasonably provide enablement for the generic recitation of any polypeptide providing the functional characteristics noted in a)-d). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

Claims 174, 184-187 and 193 are drawn to any polypeptides or polypeptide fragments which provides for the functional characteristics of elements a)-d) or aminopeptidase activity. Thus, the claims are akin to a single means claim, i.e., where a means recitation does not appear in combination with another recited element of means. Such is subject to an undue breadth rejection under 35 USC 112, first paragraph, see in particular MPEP 2164.08(a) and In re Hyatt,

708F.2d 712, 714, 715 (218 USPQ 195, 197) (Fed. Cir. 1983) where a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor. When claims depend on a recited property, a fact situation comparable to Hyatt is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. In this case only SEQ ID NO:2 is disclosed.

Moreover, as to claims 174, 184-187, 193, the skilled artisan readily recognizes that protein chemistry is an unpredictable area of biotechnology. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition, see in particular Skolnick et al., Trends in Biotech., 18(1):34-39, 2000. For example, Choh et al., of record teaches a panel of amino acid substitutions which produce proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of conserved structural components to both biological function and immunological recognition. The skilled artisan also recognizes that immunological responses depend upon the structural characteristics (conformation) of the particular protein (amino acid sequence) targeted. Jenkins et al., of record further teaches the unpredictable nature of hybridization in that there exists multiple variability in hybridizing conditions and the ability of divergent sequences to hybridize based on the length of the sequences, mismatch base pairing, temperature and unique binding characteristics of the sequences. Thus, the artisan could not a

priori determine those sequences capable of hybridization at any given set of conditions which also shared the functional constraints of the peptides claimed.

In addition, claim 188 recites a method of producing the polypeptide, yet as set forth above, because the structural characteristics required to be produced remain in question, the artisan would be required to perform further undue experimentation to first determine those peptides which correlate to the specifications of the claims and then determine an adequate means of producing the peptide, including either its sequence structure or the microorganism capable of its production.

Thus, in view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives and fragments encompassed by the claims, one skilled in the art would be forced into further undue experimentation in order to determine those peptides which correlate to the recited functional characteristics of the claimed genus and a method of producing and recovering such in order to practice the claimed invention.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 188 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 188 is rejected, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the strain or source (of micro-organism) required to produce a supernatant comprising the polypeptide of claim 170.

Claim 188 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: those steps comprising "cultivating" suitable to produce a supernatant comprising the polypeptide from any particular strain or micro-organism.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 170, 174, 177, 180, 184-185, 188, 189, 193, 196 and 199 are rejected under 35 U.S.C. 102(b) as being anticipated by Nishizawa et al., J. Biol. Chem., 269:13651-55, 1994.

As previously set forth, Nishizawa teach a *S. cerevisiae* aminopeptidase which hybridizes with SEQ ID NO:1 as the Nishizawa sequence encodes residues 255-264 of SEQ ID NO:2. This 30 mer has a Tm=87 degrees C based on the formula Tm= 4(G+C) + 2(A+T) and as it meets such characteristics is expected to have aminopeptidase activity, absent factual evidence to the contrary. As the Tm is above the medium and high temperature stringency, the sequence

inherently hybridizes under medium and high stringency conditions of 42 degrees C, absent factual evidence to the contrary. Thus, the sequence anticipates the claimed invention, see in particular residues 1180-1209 of the Nishizawa nucleic acid sequence.

Applicants argue that the sequences are not expected to hybridize under the noted conditions and that thus the reference fails to teach the claimed invention.

Applicant's arguments filed 1-23-02 have been fully considered but are not persuasive. The issue is whether or not the sequences of Nishizawa share the characteristics or are the same as the claimed invention, i.e., whether or not they can be distinguished. It has been established by the courts that "the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product, see in particular MPEP 2112, In re Fitzgerald, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)). Further, it is noted that the courts have held that when the prior art product reasonably appears to be the same as that claimed, but differs by process in which it is produced, a rejection of this nature is eminently fair and the burden is upon the appellants to prove, by comparative evidence, a patentable difference (*In re Brown*, 173 USPQ 685). Applicants have not met this burden by the statement that hybridization would not be expected. In contrast, based on the very high predicted Tm and similar melting and hybridization conditions, as exemplified for example by Jenkins et al., of record for determining hybridization conditions, temperatures, and hybridizing sequences, it is established that the sequences of Nishizawa as set forth would be expected to hybridize to SEQ

ID NO:1 or its complement and that the sequences of the prior art product would meet the limitations of the claimed invention. Thus is reasonable and rational evidence tending to show inherency. Thus, Applicant's have the burden of showing an unobvious difference.

Status of Claims

10. No claims are allowed.

11. Claims 171-173, 175-176, 178-179, 181-183, 190-192, 194-195, 197-198, 200, 201 and 206 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. Claims 202-205 are objected to under 37 CFR1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
April 8, 2002

Gary L. Kunz
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